REMARKS

Claims 2-37 are pending. Claims 3, 4, 10, 12-21, 24, 25 and 35-37 are withdrawn from consideration as being drawn to a nonelected invention and claims 6-8 and 11 are withdrawn from consideration as being drawn to a nonelected species.

No amendments to the claims are made herein and no new matter has been added.

Applicants respectfully request entry of the present Response and consideration of Applicant's arguments by the Examiner, particularly in view of the fact that no amendments to the claims have been made.

Applicants reserve their right to prosecute the subject matter of any canceled claim, any amended claim, any withdrawn claim or any unclaimed subject matter in one or more related applications.

I. The Rejection of Claims 2, 5 and 9 Under 35 U.S.C. § 103(a)

Claims 2, 5 and 9 remain rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over WO 02/10137 A2 to Bhagwat *et al.* ("Bhagwat") in view of U.S. Patent No. 6,949,580 B2 to Hale *et al.* ("Hale"). In particular, the Examiner has stated that Bhagwat teaches that indazole derivatives of formula I inhibit JNK (a protein kinase) and that Hale teaches that protein kinase inhibitors are useful for treating ocular diseases, such as macular degeneration. Applicants disagree and respectfully traverse this rejection.

As stated in Applicant's previous Response filed on December 19, 2007 in connection with the present application, Hale does not teach that kinase inhibitors in general are useful for treating ocular diseases, but rather only teaches that KDR family kinases are useful as targets for treating such diseases (*see* Hale at column 21, lines 30-44). In addition, Hale provides a specific definition for "JNK-mediated conditions," which does not include ocular diseases or macular degeneration (*see* Hale at column 21, lines 1-22) and further teaches that kinases have distinct differences in how their pathways are activated, specifically pointing to the differences between the activation of the JNK and ERK pathways (*see* Hale at column 1, lines 31-40).

In response to Applicant's arguments, the Examiner has stated that the invention of Hale relates to protein kinase inhibitors, in general, for the treatment of disease states related to protein kinase inhibitors and that macular degeneration is disclosed to be a disease mediated by KDR, which along with JNK are both protein kinases. The Examiner has further stated that the compounds disclosed by Hale, which are protein kinase inhibitors, are taught

to be useful in the treatment of all diseases-mediated by various protein kinases, such as JNK, ERK, and KDR, and that the compounds are useful in every JNK, ERK, or KDR-mediated disease.

Applicants understand the Examiner's reasoning to be that because Hale discloses that the compounds taught therein inhibit multiple protein kinases and are useful for treating any kinase-mediated disease, that any compound with activity against a single kinase would reasonably be expected to treat any kinase-mediated disease. More specifically, Applicants understand the Examiner's reasoning to be that: (i) Hale teaches that the compounds disclosed therein inhibit KDR and, thus, treat macular degeneration; (ii) Hale teaches that the compounds disclosed therein also inhibit JNK; (iii) thus, any compound that is taught to inhibit JNK must also inhibit KDR and treat macular degeneration.

Applicants respectfully disagree with such reasoning and submit that Hale does not provide any nexus between JNK and macular degeneration. Hale merely teaches that the particular compounds described therein inhibit multiple kinases, one of which is associated with macular degeneration. Indeed, the disclosure of Hale specifically highlights the fact that individual kinases are associated with different disease sets. Notably, KDR and JNK are even in different kinase families, wherein KDR is a tyrosine kinase receptor and JNK is a serine/threonine kinase (*see* Hale at column 1, lines 24-31 and column 2, line 34).

Applicants note that Bhagwat teaches that the compounds disclosed therein are selective JNK inhibitors. Again, Hale itself notes the distinct differences in the activation of kinase pathways, specifically pointing to the differences between the activation of the JNK and ERK pathways (*see* Hale at column 1, lines 31-40). Accordingly, Applicants respectfully submit that Hale does not provide any reason as to why one of ordinary skill in the art would use a JNK inhibitor for the treatment of macular degeneration or would have a reasonable expectation that such treatment would be successful. ([T]here must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." (*In re Kahn*, 441 F. 3d 977, 988 (CA Fed. 2006) cited with approval in *KSR International Co. v. Teleflex Inc.* 127 S.Ct. 1727 (2007)). Notably, although a rigid application of the teaching, suggestion, motivation test was rejected by the Supreme Court in *KSR*, the Federal Circuit has again recently approved of a flexible teaching, suggestion, motivation test in order to assure that the test for obviousness proceeds on the basis of evidence as statutorily required. *Ortho-McNeil Pharmaceuticals, Inc. v. Mylan Laboratories*, 520 F.3d 1358, 1365 (Fed. Cir. March 31, 2008).

The Examiner has further stated that Hale states that "any protein kinase inhibitor is useful to treat any protein kinase-mediated condition" (citing Hale at col. 19, lines 30-35). Applicants have reproduced this portion of Hale below (emphasis added):

> The protein kinase inhibitors of this invention, or pharmaceutical salts thereof, may be formulated into pharmaceutical compositions for administration to animals or humans. These pharmaceutical compositions effective to treat or prevent a protein kinase-mediated condition which comprise the protein kinase inhibitor in an amount sufficient to detectably inhibit protein kinase activity and a pharmaceutically acceptable carrier, are another embodiment of the present invention.

Applicants respectfully submit that this disclosure of Hale does not state that any protein kinase inhibitor is useful to treat any protein kinase-mediated disease as suggested by the Examiner, but rather states that the protein kinase inhibitors and pharmaceutical compositions specifically taught by Hale are effective to treat a protein kinase-mediated condition.[1]

Applicants note that the Examiner has stated that this is a typical genus/species situation. It is unclear what the genus/species relationship referred to is and clarification is respectfully requested. In any event, Applicants note that the Federal Circuit has consistently held that the disclosure of a genus does not necessarily render obvious any species falling within the genus. *In re Baird*, 16 F.3d 380, 382-383 (Fed. Cir. 1994); *In re Jones*, 958 F.2d 347, 350 (Fed. Cir. 1992).

For the reasons set forth above, Applicants respectfully submit that a *prima facie* case of obviousness has not been established because no reason has been provided as to why one of ordinary skill in the art would use the compounds of the pending method claims for the treatment of macular degeneration. Without such a reason, Applicants respectfully submit that a proper *prima facie* case of obviousness has not been established. *Id.*

Accordingly, Applicants submit that the rejection of claims 2, 5 and 9 under 35 U.S.C. § 103(a) has been overcome and should be withdrawn.

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[1] Applicants have refrained from addressing whether or not such disclosure is actually enabling as it does not seem necessary to do so at this time.

II. The Rejection of Claims 22, 23 and 26-34 Under 35 U.S.C. § 103(a)

Claims 22, 23 and 26-34 remain rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Bhagwat and Hale in view of U.S. Patent No. 6,204,270 B1 to Ron *et al.* ("Ron") and Applicant's alleged admission of the prior art.

Because, for the reasons set forth above, Hale does not provide any reason as to why one of ordinary skill in the art would use the compounds of the pending method claims to treat macular degeneration, Applicants respectfully submit that a proper case of *prima facie* obviousness over Bhagwat and Hale in view of Ron has not been established. *Id.*

Accordingly, Applicants submit that the rejection of claims 22, 23 and 26-34 under 35 U.S.C. § 103(a) has been overcome and should be withdrawn.

Conclusion

Applicants respectfully request that the above remarks be entered in the present application file. No fee is estimated to be due in connection with this Response other than that due in connection with the Request for Continued Examination; however, in the event that any additional fee is determined to be due, please charge the required fee to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

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